KIT gene

KIT proto-oncogene receptor tyrosine kinase

Normal Function

The *KIT* gene provides instructions for making a protein that belongs to a family of proteins called receptor tyrosine kinases. Receptor tyrosine kinases transmit signals from the cell surface into the cell through a process called signal transduction. The KIT protein is found in the cell membrane of certain cell types where a specific protein, called stem cell factor, attaches (binds) to it. This binding turns on (activates) the KIT protein, which then activates other proteins inside the cell by adding a cluster of oxygen and phosphorus atoms (a phosphate group) at specific positions. This process, called phosphorylation, leads to the activation of a series of proteins in multiple signaling pathways.

The signaling pathways stimulated by the KIT protein control many important cellular processes such as cell growth and division (proliferation), survival, and movement (migration). KIT protein signaling is important for the development of certain cell types, including reproductive cells (germ cells), early blood cells (hematopoietic stem cells), immune cells called mast cells, cells in the gastrointestinal tract called interstitial cells of Cajal (ICCs), and cells called melanocytes. Melanocytes produce the pigment melanin, which contributes to hair, eye, and skin color.

Health Conditions Related to Genetic Changes

core binding factor acute myeloid leukemia

gastrointestinal stromal tumor

Mutations in the *KIT* gene are the most common genetic changes associated with gastrointestinal stromal tumors (GISTs). GISTs are a type of tumor that occurs in the gastrointestinal tract, most commonly in the stomach or small intestine. In most cases, these *KIT* gene mutations are acquired during a person's lifetime and are called somatic mutations. Somatic mutations, which lead to sporadic GISTs, are present only in the tumor cells and are not inherited. Less commonly, *KIT* gene mutations that increase the risk of developing GISTs are inherited from a parent, which can lead to familial GISTs.

KIT gene mutations associated with GISTs create a protein that no longer requires binding of the stem cell factor protein to be activated. As a result, the KIT protein and the signaling pathways are constantly turned on (constitutively activated), which increases the proliferation and survival of ICCs, leading to GIST formation.

piebaldism

At least 69 *KIT* gene mutations have been identified in people with piebaldism. This condition is characterized by white patches of skin and hair caused by a lack of melanocytes. The mutations responsible for piebaldism lead to a nonfunctional KIT protein. The loss of KIT signaling is thought to disrupt melanocyte migration and proliferation during development, resulting in patches of skin that lack pigmentation.

other cancers

Somatic mutations in the *KIT* gene have been identified in several cancers. *KIT* gene mutations are involved in some cases of acute myeloid leukemia, which is a cancer of a type of blood cell known as myeloid cells, and sinonasal natural killer/T-cell lymphoma (NKTCL), another blood cell cancer that occurs in the nasal passages. In addition, some people with seminoma, a type of testicular cancer, have a *KIT* gene mutation. The genetic changes involved in acute myeloid leukemia and seminomas lead to a KIT protein that is constitutively activated. The constant signaling causes overproliferation of the cells that make up these tumors. It is unclear how the *KIT* mutations in NKTCL are involved in the condition.

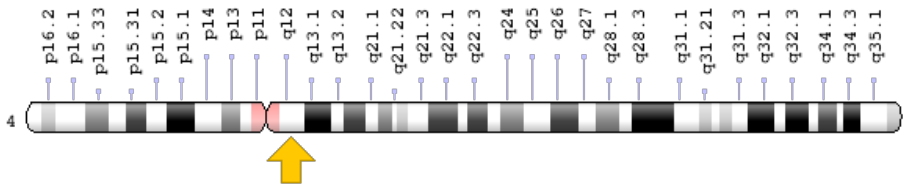
other disorders

KIT gene mutations are also involved in mastocytosis, which represents a group of related conditions. These conditions are characterized by an overgrowth of mast cells, which are cells that trigger inflammation during an allergic reaction or an infection. Accumulation of excess mast cells in the skin causes a condition called urticaria pigmentosa, and accumulation in additional organs leads to systemic mastocytosis. The *KIT* gene mutations involved in this group of conditions lead to a constitutively activated KIT protein, which causes the overgrowth of mast cells.

Chromosomal Location

Cytogenetic Location: 4q12, which is the long (q) arm of chromosome 4 at position 12

Molecular Location: base pairs 54,657,928 to 54,740,715 on chromosome 4 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- C-Kit
- CD117
- KIT_HUMAN
- mast/stem cell growth factor receptor Kit
- p145 c-kit
- PBT
- piebald trait protein
- proto-oncogene c-Kit
- proto-oncogene tyrosine-protein kinase Kit
- SCFR
- tyrosine-protein kinase Kit
- v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog
- v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene-like protein

Additional Information & Resources

Educational Resources

- Developmental Biology (sixth edition, 2000): The RTK Pathway
  https://www.ncbi.nlm.nih.gov/books/NBK10043/#A1053

Genetic Testing Registry

- GTR: Genetic tests for KIT
  https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=3815%5Bgeneid%5D

Scientific articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28KIT%5BTI%5D%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+720+days%22%5Bdp%5D

OMIM

- LEUKEMIA, ACUTE MYELOID
  http://omim.org/entry/601626
- MAST CELL DISEASE
  http://omim.org/entry/154800
- V-KIT HARDY-ZUCKERMAN 4 FELINE SARCOMA VIRAL ONCOGENE HOMOLOG
  http://omim.org/entry/164920

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/KITID127.html
- HGNC Gene Family: CD molecules
  http://www.genenames.org/cgi-bin/genefamilies/set/471
- HGNC Gene Family: Immunoglobulin like domain containing
  http://www.genenames.org/cgi-bin/genefamilies/set/594
- HGNC Gene Family: Receptor Tyrosine Kinases
  http://www.genenames.org/cgi-bin/genefamilies/set/321
- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=6342
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/3815
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